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DISCUSSION

Diseases are Not Adaptations and Neither are Their Causes

A Response to Ardern's "Dysfunction, Disease, and the Limits of Selection" (*Biological Theory* 13:4–9, 2018)

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Abstract
In a recent article in this journal, Zachary Ardern criticizes our view that the most promising candidate for a naturalized criterion of disease is the "selected effects" account of biological function and dysfunction. Here we reply to Ardern's criticisms and, more generally, clarify the relationship between adaptation and dysfunction in the evolution of health and disease.

Keywords Disease · Dysfunction · Function · Selected effects

In a recent article in this journal Zachary Ardern (2018) has questioned our view that the best prospect for introducing an objective, biological criterion into a definition of disease is to make use of a "selected effects" account of biological function and dysfunction (Griffiths and Matthewson 2018). Ardern argues that (1) small effective population sizes in hominin lineages make it unlikely that the genetic bases of disease are the result of natural selection, (2) that both the genetic basis of disease and the selective history of disease variants are likely to be "experimentally intractable" (2018, p. 4), and (3) that some diseases have been positively selected for, or at least have not been selected against.

We welcome Ardern's introduction of more biological detail into the debate over definitions of disease, something we called for in our paper. However, his criticisms reveal that he has misunderstood both our specific proposal and the relationship between adaptation and disease more generally. Diseases are not adaptations. Nor, except in some specific cases, are the *causes* of disease adaptations. Moreover, as we will demonstrate below, a causal factor that makes the difference between a normal, functional phenotype and its dysfunctional alternatives need not be an adaptation for producing the normal phenotype. When these three points are clarified, it will be seen that the genomic findings Ardern introduces to the discussion are entirely consistent with our view.

Beyond any specific disagreement we may have with Ardern, this is an opportunity to clarify the relationship between adaptation and disease and to highlight what appear to be common misapprehensions about that relationship. We begin by restating the central claims made (and not made) in our paper, and then turn to address Ardern's three points.

What We Claimed About Dysfunction and Disease

Griffiths and Matthewson (2018) outlined the selected effects account of function and dysfunction, and defended its use as the naturalistic component in definitions of disease.

The Selected Effects Account of Function and Dysfunction

The selected effects account of biological function is summed up in a pithy quote by Karen Neander:

> 'biological proper functions are effects for which traits were selected by natural selection' (Neander [1991],

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p. 168). (quoted in Griffiths and Matthewson 2018, p. 304)

A trait can have any number of effects, but only the effects that play a role in explaining the evolutionary success of the trait are selected effects functions of the trait. Hemoglobins, for example, deliver oxygen to tissues and also allow photoplethysmographic heart rate monitors to measure pulse. Hemoglobins were *selected for* (Sober 1984) delivering oxygen to tissues, and this is therefore one of their selected effect functions. However, whilst there was *selection of* (Sober 1984) a molecule that is used to measure pulse, it is not a proper function of that molecule to facilitate those measurements. This distinction between effects that played a causal role in natural selection (selection for) and the rest (selection of) is at the heart of the selected effects theory of function, and the canonical statements of the theory include this requirement (e.g., Millikan 1984, p. 28; Neander 1991, p. 174).

On the selected effects approach, *dys*function is the *failure* of some structure or behavior to perform its proper function. A trait can fail to perform its proper function either because it is intrinsically unable to do so, or because external circumstances interfere with its operation. For example, hemoglobin may fail to deliver oxygen to the tissues either because of a structural abnormality in the molecule, or because the atmosphere contains too much carbon monoxide.[1]

What We Did Not Claim

Griffiths and Matthewson (2018) argued that the strongest candidate for a nonevaluative criterion in definitions of disease is a requirement that the diseased trait exhibit selected effects dysfunction—it fails to perform the function for which it is an adaptation. As part of our argument we criticized the popular view that the strongest candidate is the alternative, so-called "biostatistical," definition of function and dysfunction. (e.g., Boorse 1977; Kingma 2010; Hausman 2012; Schwartz 2014).

It is important to be clear what we did *not* claim. First, we did not claim to have shown that any analysis of disease *must* contain an objective, nonevaluative criterion. Our arguments were primarily addressed to people who already advocate a "naturalist" account of disease (one that contains a nonevaluative criterion): "we aim to convince naturalists to seriously consider the selected effect account of function. We do not argue that those who reject naturalism must adopt a selected effects account!" (Griffiths and Matthewson 2018, p. 303). However, we did take our arguments to be relevant to the naturalist/anti-naturalist debate in an indirect way: "Our arguments are relevant to anti-naturalists because, as we show below, many of them take a refutation of the biostatistical view of function to be *ipso facto* a refutation of naturalism" (p. 303).

Second, we did not argue that the selected effects account of dysfunction is a complete account of disease—"we do not offer an overall account of the concept of disease" (p. 303). In fact, our article was sympathetic to Jerome Wakefield's well-known "hybrid" definition of disease (Wakefield 1992, 2007) This combines a naturalist criterion – selected effects dysfunction—and a normative criterion—evaluative harm. Diseases are "harmful dysfunctions." But it was beyond the scope of our article to defend this specific account against alternatives.

Third, we did not argue that selected effects functions are the only legitimate functions to invoke in biology, or even in medicine:

> Nothing we say in this article should be taken to suggest there is a single correct account of biological function. Both authors are pluralists: we think there are a number of legitimate notions of function at play in the biological sciences, each with advantages in different contexts …. Perhaps more than one account will be needed, even in medicine alone. (Griffiths and Matthewson 2018, p. 303)

Fourth, we did not make claims regarding what can and cannot *cause* disease. We were concerned with the question of what disease *is* rather than what leads to disease, or what protects us against disease, or what explains disease. In the same way that being warm-blooded is part of the traditional definition of mammal, but not a *cause* of being a mammal, selected effects dysfunction is part of the definition of, but not a cause of, being a disease. This conflation between the tasks of definition and explanation is easy to make in philosophical analysis. However, in this particular instance, the risk of confusion is increased, since some diseases actually have evolutionary causes or explanations. Nevertheless, we must keep that issue separate from the question of what constitutes disease.

Readers new to this literature may be wondering at this point what turns on the definitional issue, so to quickly clarify: The philosophy of medicine has devoted vast efforts to the biostatistical account of function, and we think this is a mistake. It has skewed debate about the disease concept, as failures of the biostatistical account have been viewed as failures of naturalism regarding disease. Most importantly in

[1] Neander argues that only in the first case should we say that a trait is "dysfunctional" (Neander 1995). One might say that a trait that fails to perform its function because of external conditions is "dysfunction*ing*" but not in itself "dysfunction*al*." On our reading, Millikan is concerned with both kinds of failure since she says that a trait can only perform its proper function when it operates in "Normal" conditions (e.g., 1984, pp. 33–34). We do not think this distinction is significant in our dispute with Ardern and will use "dysfunction" indifferently to refer to both kinds of failure to perform function.

our view, our paper attempted to move away from the style of conceptual analysis that tests analyses against intuitions about whether some case should be called "dysfunction" or "disease." We tried instead to give substantive reasons for adopting one concept of dysfunction rather than another, reasons that could justify rejecting what seems intuitive in some instances.

Ardern's Critique

Now we have clarified the views that Ardern is criticizing, we can examine his criticisms.

The Key Misunderstanding: Constitution versus Causation

Ardern's primary objection to the view that disease involves selected effects dysfunction is that if it is true, then only genetic variants that have a selected effects function can *cause* disease. For example, he writes that:

> A selected effects account of disease assumes that diseases require disorder and hence dysfunction in the causative traits. (Ardern 2018, p. 5)

> The data implies, however, that many [*genetic*] elements that this account would class as nonfunctional are still relevant to disease processes. Disease would not then necessarily be a *result of dysfunction*, and could not be grounded in selected effects. (Ardern 2018, pp. 6, 7; our emphasis)

> If the assumption that disease is dependent upon dysfunction is retained as it is generally in the current literature, then the proponent of selected effects must show that traits *underlying* disease are dysfunctional. (Ardern 2018, p. 5; our emphasis)

However, proponents of a selected effects account do *not* need to show this. They do not say that disease phenotypes are a "result of dysfunction" in the sense of being caused by dysfunctional traits. It is the disease phenotype itself that is dysfunctional on this account, not the causes of that phenotype. Hence the account does not require that the *causes* of impairment are adaptations, let alone that they are dysfunctional adaptations. A broken leg is a pathological phenotype because the adaptive functions of bone and blood vessels are disrupted; the evolutionary history of the *causes* of the broken leg is simply irrelevant. The leg might have been broken by a falling rock, and rocks don't have adaptive functions.

Ardern reiterates this argument when he says that, "In light of the arguments that follow regarding the apparent insufficiency of selection in *accounting for disease variants*, it may be that proponents of selected effects in biology should drop the assumption that disease requires dysfunction. Perhaps, for instance, junk DNA is able to accumulate mutations..." (Ardern 2018, p. 5; our emphasis).

Once again, however, the selected effects account of dysfunction does not involve selection "accounting for disease variants." Natural selection explains the functional traits that are impaired by disease variants, but it need not explain the variants that cause impairment of those functional traits. To return to our previous example, a broken leg caused by a falling rock is a dysfunctional phenotype. But that is not because there was selection for falling rocks. There was selection for functional legs, whose function can be impaired by the impact of falling rocks. The genetic causes that Ardern focuses on are no different from these environmental causes—rocks and mutations can both render phenotypes dysfunctional without rocks or mutations themselves being dysfunctional.

The claim that disease-causing mutations have been selected to cause disease is not very plausible, and although it seems the natural reading of the quoted passages we are reluctant to believe that Arden really attributes this claim to us. So let us consider another idea that Ardern may be attributing to us – one that it is less obviously problematic but which, nevertheless, we do not believe and which is not a consequence of the selected effects account of dysfunction.

The less obviously problematic view that Arden may be attributing to us is that selection must account for the *normal state* of traits whose variations cause disease. On this reading, the causes of disease necessarily fail to perform their proper function when they cause disease. Take, for example, the hundred or so well-replicated genetic variations that are linked to Type II diabetes. On this reading of Ardern, he alleges that the selected effects account of dysfunction implies that if Type II diabetes is a disease then the normal (wild type) variant of each of these hundred or so loci must have evolved by natural selection for its role in normal insulin metabolism.

However, although it is less obviously mistaken, this view is still mistaken and we did not advocate it in our (2018) article. A selected effects account of dysfunction does not require that selection explains the normal state of each cause whose variation can induce dysfunction. The selected effects account implies that any phenotype that can become dysfunctional must be an adaptation. It does not imply that anything that can cause a phenotype to become dysfunctional must be an adaptation for producing the *normal* phenotype.

Imagine that Arden were to take the same approach to environmental causes of disease that, on this reading, he takes to genetic causes. The absence of asbestos in the lungs was not selected to improve lung function. The disease of asbestosis did not occur before the industrial production of asbestos and so played no role in the evolution of lungs.

By analogy with what Ardern says about genetic causes of disease, this would imply that asbestosis is not a condition in which the lungs are dysfunctional. But this is obviously wrong in the environmental case, and it is no more correct in the genetic case. On the selected effects account of dysfunction what matters is *whether* the lungs can perform their evolved function, not *why* they cannot perform it.

Our disagreement with Ardern is not over the empirical question of whether wild type alleles at loci that impair function are adaptations to produce that function. Our disagreement is over whether that question is *relevant*. The selected effects account of dysfunction does not require that each cause of dysfunction must itself have an adaptive function.

Selection and the Human Genome

In the last section we saw that Ardern targets the claim that the *causes* of disease are adaptations. But the selected effects account of function/dysfunction does not make this claim. As a result, the empirical data Ardern marshals to support his case misses the mark. The most significant place where this arises is in his section "Modern Histories and Selection in the Hominin Lineage."

Ardern writes that:

> Peter Godfrey-Smith (1994, pp. 356, 357) recognizes that the modern history approach does "make substantial biological commitments." This leaves it open for biological counterexamples based on what selection is actually achieving in populations. Specifically, as he says, "perhaps many traits around now are not around because of things they have been doing. Then many modern-historical function statements will be false." This empirical claim will be argued below. (2018, p. 5)

Ardern then presents data intended to show that because of small hominin effective population sizes, very little of the variation accumulated in hominin genomes since their divergence from chimpanzees has been subject to selection. In particular, many loci housing genetic variations that cause disease have not been subject to purifying selection. This extended discussion is the empirical heart of his paper.

As an aside, we think that Ardern overstates the strength of evidence for his empirical claim. There is significant support for the opposite view, and evidence that adaptation has acted on the genetic basis of complex, polygenic traits in humans in recent history (Field et al. 2016).[2] But there is no need to settle this dispute here, since even if we grant Ardern his empirical claims about human evolution, the argument founded on them does not undermine the selected effects account of dysfunction as a component of an account of disease.

The data Ardern presents supports the view that when diseases have genetic causes, those genetic variants have likely accumulated by drift, because selection has not been strong enough to remove them. This means there is no selective story about why the disease variant occurs. But, for the reasons given in the previous section, this is not something the selected effects account need care about. The selected effects account is silent regarding the causes of dysfunction—it only says that the affected trait must itself be dysfunctional. If a functional trait is disrupted by a mutation then whether the mutation is germ line or somatic, and whether it is ancient or brand-new, the trait becomes dysfunctional. The evolutionary history of the mutation is not relevant.

What Arden actually needs to show is that the functional phenotypes that are impaired by these mutations have not been subject to recent selection. He does not attempt to show this, and for good reason, as in many cases it would be highly implausible.

Consider, for example, Type I diabetes. If Ardern is to challenge the claim that Type I diabetes is a dysfunctional phenotype, it is not enough to show that, for example, selection has not acted against variants of the ISN gene that cause Type I diabetes. Type I diabetes is dysfunctional because there has been recent selection in the hominin lineage for *normal insulin production*, which is the phenotype impaired in Type I diabetes. The evidence for this does not come from evolutionary genetics but from the observed heritability of Type I diabetes and the life expectancy and fecundity of people with untreated Type I diabetes. If Ardern is right, and we cannot find any genetic loci that are implicated in insulin metabolism and which show evidence of having been subject to recent natural selection that would be surprising. But it would not undermine the direct evidence that variation in this trait is heritable and that the selection coefficient obtained by comparing people with normal insulin metabolism to those with Type I diabetes is large. However, as a matter of fact we do not need to worry about such a paradoxical discovery. The data suggests that recent increases in the prevalence of Type I diabetes result from reduced selection for normal insulin production, and hence relaxation of selection on disease variants, due to modern medical care (You and Henneberg 2016).

To see where Ardern has gone wrong, a comparison with environmental causes of disease is helpful. Type II diabetes is often the result of an obesogenic environment resulting from the industrial production and distribution of calorie-dense foods. Natural selection has, obviously, not acted to reduce the prevalence of fast-food restaurants or high-energy snack foods. Nevertheless, prolonged exposure to these foods can cause Type II diabetes. The selected effects

[2] We thank Joshua Christie for this reference.

account claims that dysfunction is present because particular endocrine systems in humans, which were selected for their ability to control blood glucose, are unable to do so in these individuals. Hence they are dysfunctional. This claim about the adaptive function of these glucose control systems is uncontroversial, and has nothing to do with whether the present causes of dysfunction in these control systems are the result of natural selection.

In the case of fast-food restaurants and high-energy snack foods it is obvious that the evolutionary history of these causes of diabetes is irrelevant to whether Type II diabetes is a dysfunctional phenotype. It is an interesting question why this point is less obvious in the case of *genetic* causes of Type II diabetes. What lends apparent plausibility to Ardern's argument when he focuses on genetic causes is that it would be genuinely surprising if, as he suggests, much or all of the genetic variation that causes disease in modern humans has been exempt from recent selection. If we were really to discover that there had been no selection at loci that account for a significant portion of the variance in Type II diabetes we would face a scientific paradox and we might hunt about for a way to resolve that paradox – "Is this trait really so bad for you? Is it really a disease?" we might ask. This lends an apparent but ultimately misleading plausibility to Ardern's suggestion that the selected effects account of dysfunction requires evidence that recent selection has favored disease-causing genetic variants. Moreover, although the selected effects account does not require this evidence, it is worth noting that, as one might expect given the obvious selective costs of diabetes, recent selection in hominin lineages does seem to have favored genetic variants that are protective against the abnormalities of insulin production found in Type II diabetes (Ségurel et al. 2013).

Ardern's marshalling of empirical data to examine a philosophical view of function is important, and we welcome this shift in the grounds of the debate. However, the evidence he presents would, if correct, only show that much of the burden of human disease is due to small hominin effective population size making it impossible to purge the population of deleterious genetic variation. We do not accept this conclusion, but even if it is correct it is entirely compatible with the "modern history" selected effects account of dysfunction and its use in definitions of disease.

Practical Issues with Identifying Selection

In a supplementary argument, Ardern claims that it is usually very hard to locate the genetic variants responsible for diseases or to demonstrate selection at those loci:

> Both the initial difficulty of finding causal variants underlying disease and the compounded difficulty in determining the (recent) selective history of particular phenotypes contribute to a pragmatic argument against a selective effects account. (Ardern 2018, p. 7)

Hence, writes Ardern:

> Whatever its other benefits, such an [*selected effect*] account simply isn't particularly useful in practice if evolutionary histories pertaining to disease generally cannot be discerned. (Ardern 2018, p. 7)

What "cannot be discerned" according to Ardern is whether and where in the genome selection has acted on specific regions involved in the development and functioning of phenotypes. But that is not what he needs to show in order to criticize the selected effects account as impractical. He needs to show that we cannot discern how selection has acted to maintain the phenotypes whose function is impaired in disease. In our (2018) article we contended that for many disease phenotypes it is reasonably clear how impairment of function reduces fitness and therefore highly plausible that selection has been at work in recent history. Returning to the example of Type II diabetes, the genetics of this disease are complex and ill-understood, just as Ardern suggests. There are over a hundred well-replicated genetic associations with this phenotype, and even taken together these associations leave most of the observed heritability of the trait unexplained (Prasad and Groop 2015). If we accept Ardern's reasoning, this should be a major challenge to our ability to determine whether Type II diabetes is dysfunctional. But it is not. It is perfectly possible to conclude that natural selection acts in favor of normal insulin metabolism and against Type II diabetes without locating the genetic loci that make the difference between these two phenotypes or documenting selection at those loci, and biologists have done just this (Ségurel et al. 2013; Little et al. 2017). Adaptive evolution can be rigorously documented at the phenotypic level without identifying the specific loci at which allele frequencies have changed: this is not controversial.

Ardern's Closing Arguments

Following these two primary criticisms, Ardern raises broader concerns regarding the use of evolution in a naturalistic criterion of disease. He first presents a series of cases where the connection between fitness and health appears to be undermined. Then he raises some more general questions regarding nonevaluative criteria of disease and health.

Examples Where Fitness and Health Purportedly Come Apart

Ardern notes that in many cases, "natural selection does not promote health" (2018, p. 7). This is correct, and advocates of evolutionary medicine have stressed the point (Nesse

2001). Ardern, however, uses this observation as an argument against defining disease wholly or partly as failure to perform an adaptive function. He describes cases in which the pathological effect of a phenotype is apparently the same as or closely linked to its adaptive function. If correct, this would obviously reduce the appeal of selected effects dysfunction as a criterion of disease. However, in each case Ardern has subtly misconstrued the relationship between adaptation and dysfunction, and his arguments provide a further opportunity to clarify this relationship.

Rather than reiterate Ardern's specific examples, we will deal with them in classes:

1. "Mismatch" cases: These are cases where a phenotype that was advantageous in ancestral environments is now disadvantageous. Since the trait is doing what it is designed to do, this raises the question of how it can be dysfunctional. The selected effects account of function deals with such cases in the way first introduced by Ruth Millikan (Millikan 1984, pp. 33–34). A trait can fail to perform its function either because of intrinsic damage or because it is not in a Normal[3] environment. The lungs of a drowning person cannot perform their function because they are in an abNormal environment—water rather than air. Similarly, the mechanisms controlling nutritional intake cannot perform their function in an abNormal environment full of engineered superfoods. Some authors may prefer to say in such cases that the trait is not dysfunctional in itself, merely *dysfunctioning* in the abNormal environment (see fn 1). For treatments of more complex mismatch cases involving evolved phenotypic plasticity see Matthewson and Griffiths (2017).

2. Disorders that enhance fitness: Ardern argues that natural selection sometimes *promotes* disease; that there are disease phenotypes which are "selected disorders." "A large class of pathologies which could be described as selected disorders are conditions that are a side effect of a trait that carried a fitness advantage" (Ardern 2018, p. 8). The best-known example of this phenomenon is sickle cell anemia, but there are many others. As Ardern notes, the selected effects theorist will appeal here to the distinction between "selection of and selection for," a distinction central to the selected effects account of function (see the first section). There is selection *of* the trait (anemia) but not selection *for* this dysfunctional trait. Ardern replies that, "[i]n biological practice the distinction will be difficult to maintain, without detailed access to selective histories" (2018, p. 9). However, Ardern gives examples where the selection history is very well understood (as in sickle cell anemia), so his skepticism must rest on his view that identifying adaptations requires understanding their genetic architecture, a claim that we refuted above.

3. Disorders involving life history trade-offs: Ardern concludes his discussion of these cases by saying, "If one disease only affects the elderly, while another has identical symptoms but tends to affect younger people, are both equally real disorders? The selected effects account implausibly says no" (2018, p. 8). This claim is surprising, since our (2018) article specifically showed that life history theory demonstrates why the selected effects account does not say "no" in such cases.

The point Ardern is making is that the same phenotypic trait may be selected for in one life-history stage, but neutral or selected against in another life-history stage.[4] One of the main errors made by critics of the selected effects account is to suppose that traits have the same functions throughout the life history of an organism, whereas in reality functions are indexed to life-history stages. Embryonic hemoglobins perform an important function in the embryo, but embryonic hemoglobins in an adult organism would be dysfunctional. The function of embryonic hemoglobins is indexed to a life-history stage. There is nothing controversial or paradoxical about this. In our article (2018), we argued that the kinds of cases cited by Ardern actually strongly support the selected effects account of dysfunction over its alternatives. To summarize the extended treatment we gave in the original paper, we define a senescent phenotype as a change in a phenotypic character where there has been no selection for the manifestation of the character state in the life-stage following the change. It is generally supposed that when character states are expressed in life-stages where they confer no advantage this is because that pattern of expression is physiologically or genetically linked to some other, advantageous trait. When the linkage is genetic, this explanation is called "antagonistic pleiotropy," a foundational idea in evolutionary medicine.

Naturalism and Values in Accounts of Disease

The final section of Ardern's paper criticizes both the idea that a stand-alone selected effects account of dysfunction can define disease (a position we do not hold: see the first section), and the proposal that the selected effects account can be supplemented by an evaluative condition, as in Wakefield's "harmful dysfunction" account of disease. This hybrid account, he tells us, needs "further work [that] consists in either teasing apart the evaluative and nonevaluative components of the model or naturalistically justifying the use of evaluative judgments" (2018, p. 8). Wakefield and his

[3] Millikan uses capitalized "Normal" to refer to the class of environments in which the trait successfully performed its adaptive function in the evolutionary past.

[4] These trade-offs are regarded in evolutionary medicine as an important evolutionary cause of disease.

critics and commentators have been engaged in this project for some decades (Wakefield 1992 has more than 1400 citations), but we admit it is not work we ourselves undertook in the paper targeted by Ardern. Directly defending naturalism was not one of our objectives in the article.

In fact, like Ardern, we do not think that the selected effects account of dysfunction is adequate as a stand-alone account of disease. In fact, we do not think it is even a complete account of dysfunction in the context of medicine. But we do think there are good reasons to include evolutionary considerations in definitions of disease. Our reasons for both of these conclusions can be found in an earlier paper (Matthewson and Griffiths 2017).

Conclusion

Ardern's arguments against using the selected effects account of dysfunction as one criterion of disease do not succeed. His introduction of data from the evolutionary genetics of human populations is to be welcomed. However, in this particular instance the arguments fail because Ardern marshals this data against a claim the selected effects account does not make: that the causes of disease must be adaptations to produce the healthy version of the disease phenotype and that these causes therefore fail to perform their adaptive function when they cause disease. This is not a commitment of the selected effects account, and so the fact that it is false in many cases is simply not relevant.

Ardern uses the same data to be skeptical of our ability to determine whether a phenotype has an adaptive function. We think he overstates the case regarding how hard it is to document selection acting on genetic variants in hominin lineages, but this dispute is not important, since once again the data are marshalled against the wrong target. Ardern argues that we cannot identify the specific genetic loci at which selection acted in the evolution of phenotypes that can become diseased. But that is not what the selected effects account requires in order to attribute function. Evidence regarding phenotypic adaptation is sufficient.

Ardern supplements these core arguments with a list of examples in which the pathological effect of a phenotype is apparently also an adaptive function of that phenotype. These cases are well-known in evolutionary medicine, and when they are more carefully described we see that they do not really have this paradoxical quality.

Once again, we are very glad Ardern has brought more empirical detail into this philosophical debate. The selected effects account of dysfunction emerges unscathed, but the discussion has, we hope, helped clarify and advance the issues at stake.

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